Figure 1. N-linked Glycoprotein Structures.

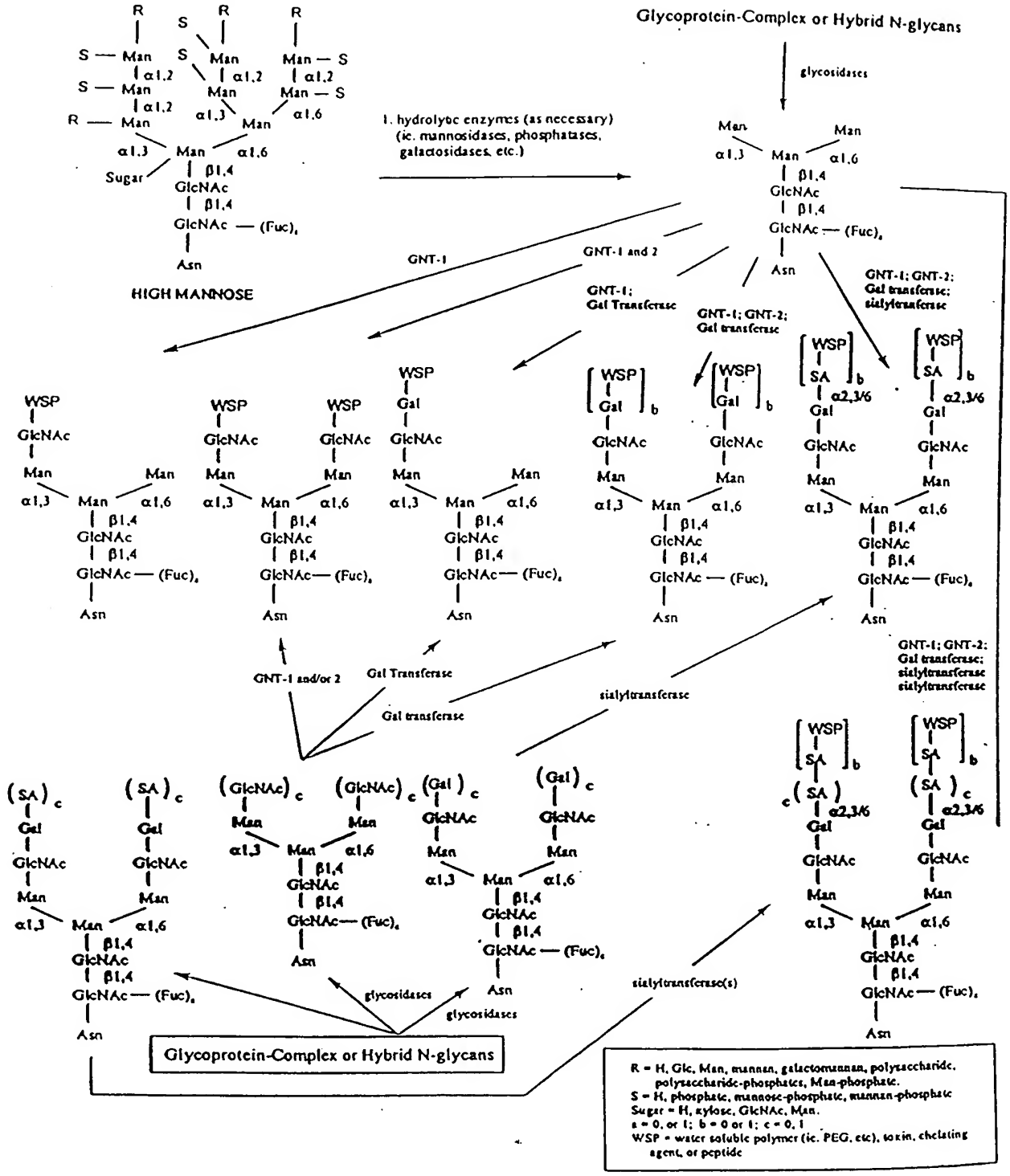


FIG. 1

Scheme 2.

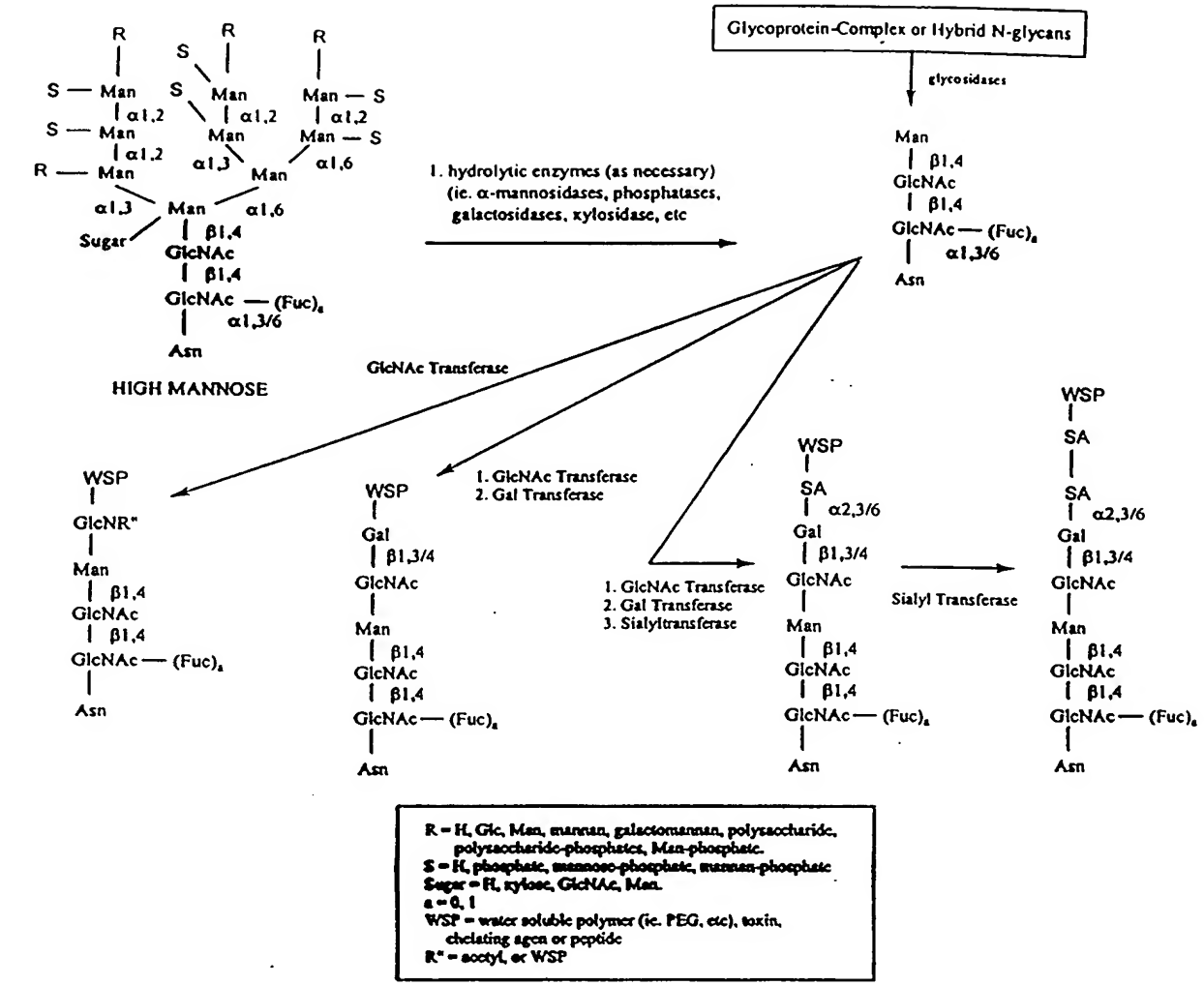


FIG. 2

Scheme 3.

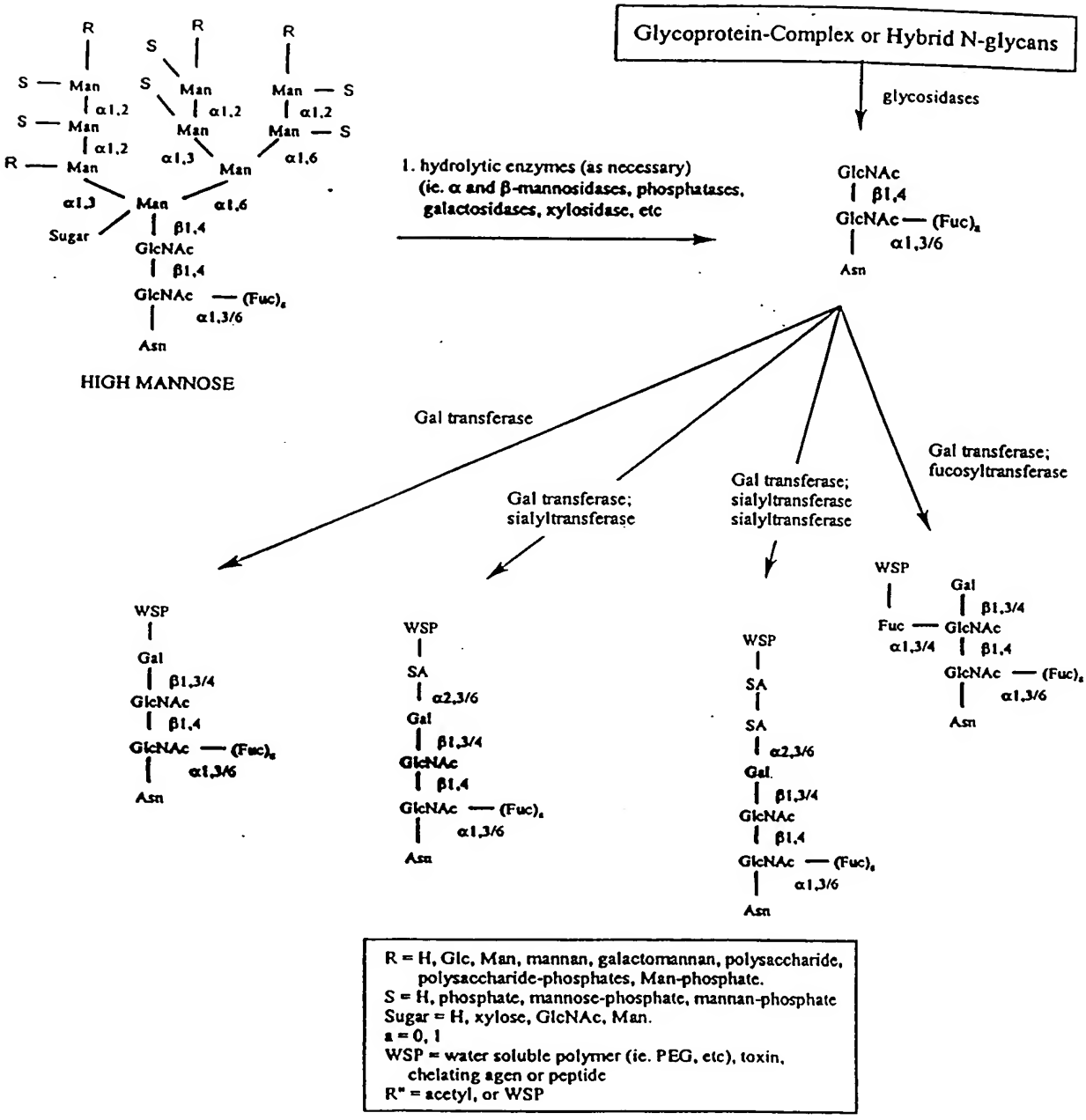


FIG. 3

Scheme 4.

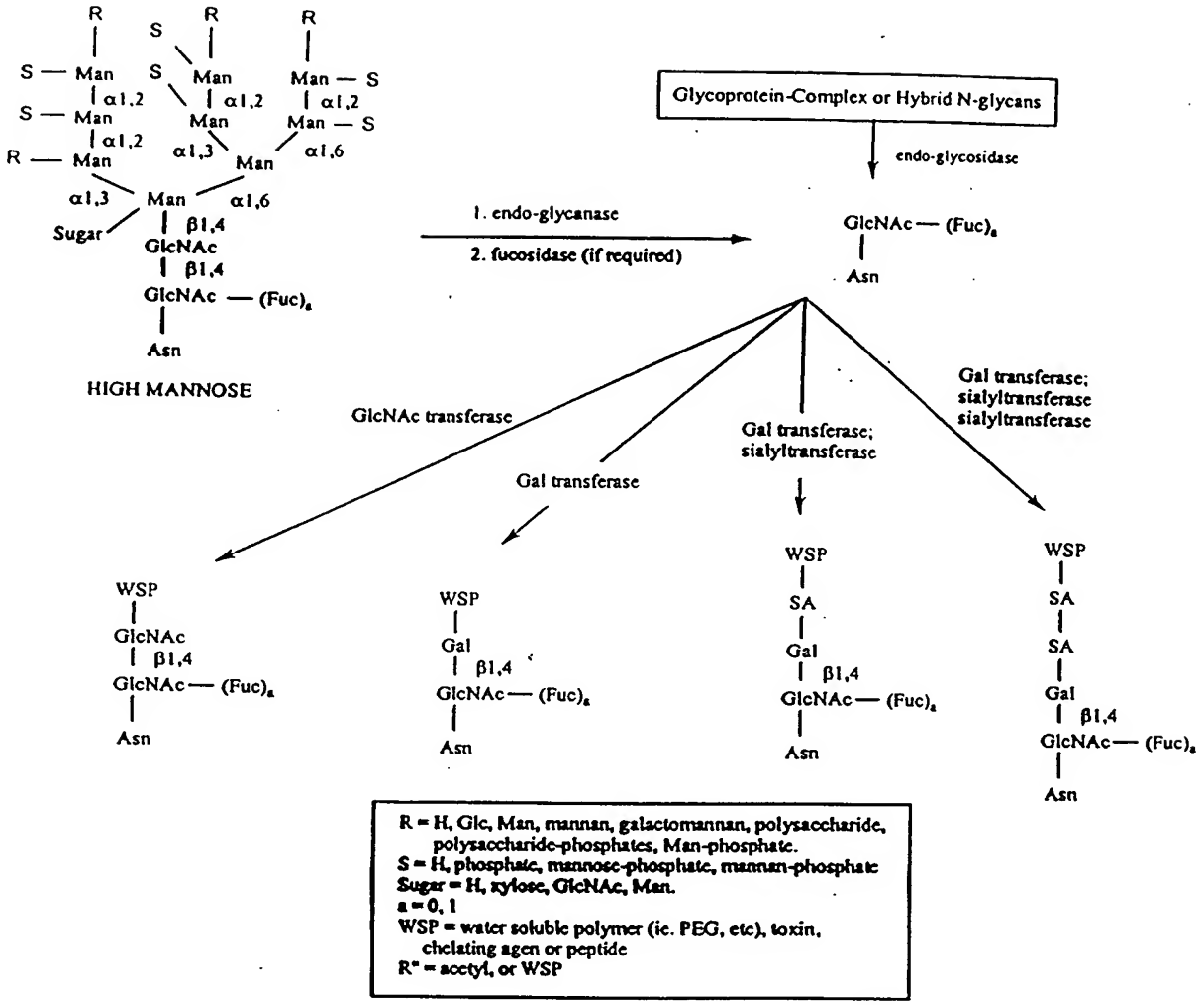


FIG. 4

Figure 5. N-linked Glycoprotein Structures.

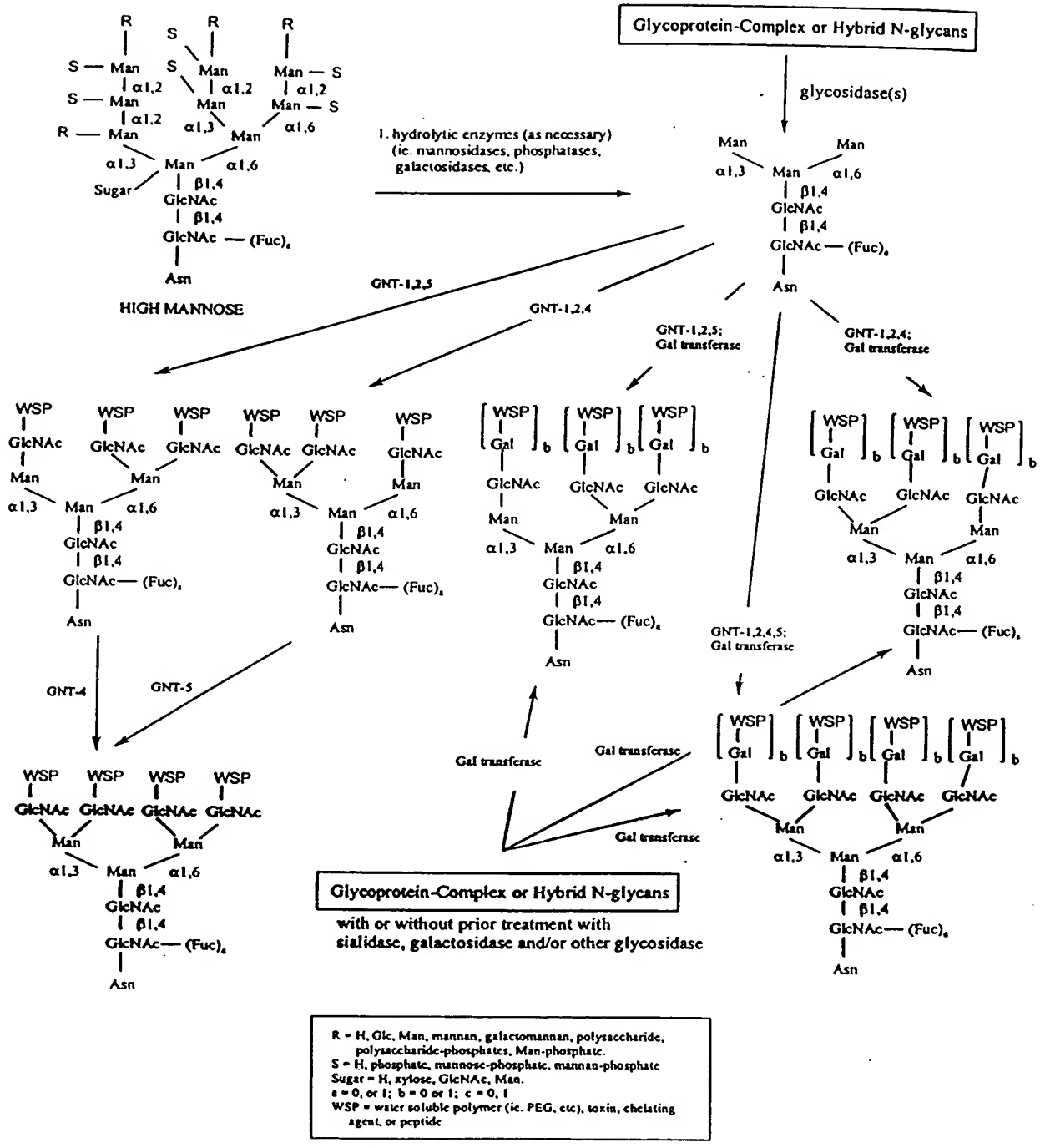


FIG. 5

Figure 6. N-linked Glycoprotein Structures.

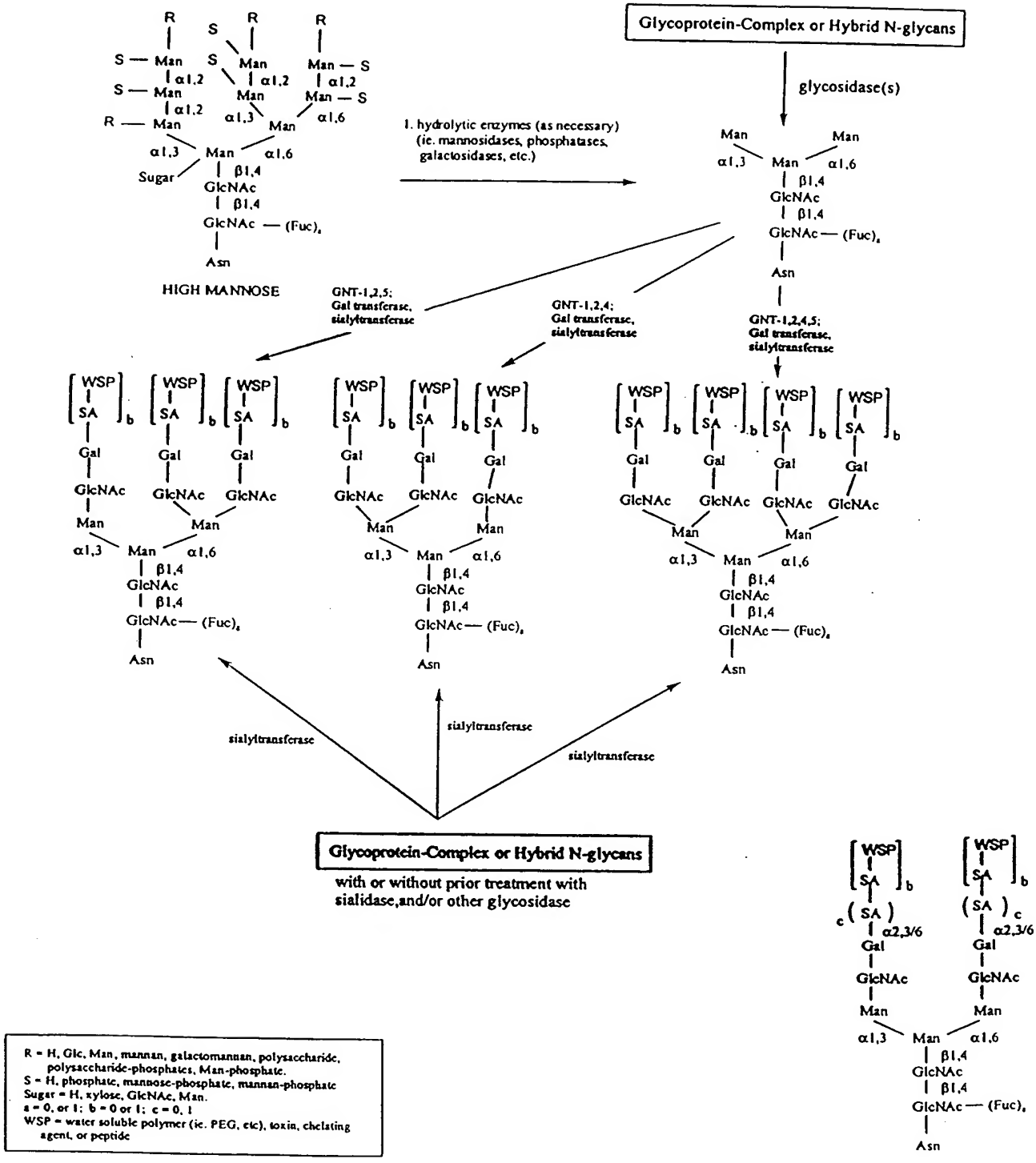


FIG. 6

Figure 7. N-linked Glycoprotein Structures.

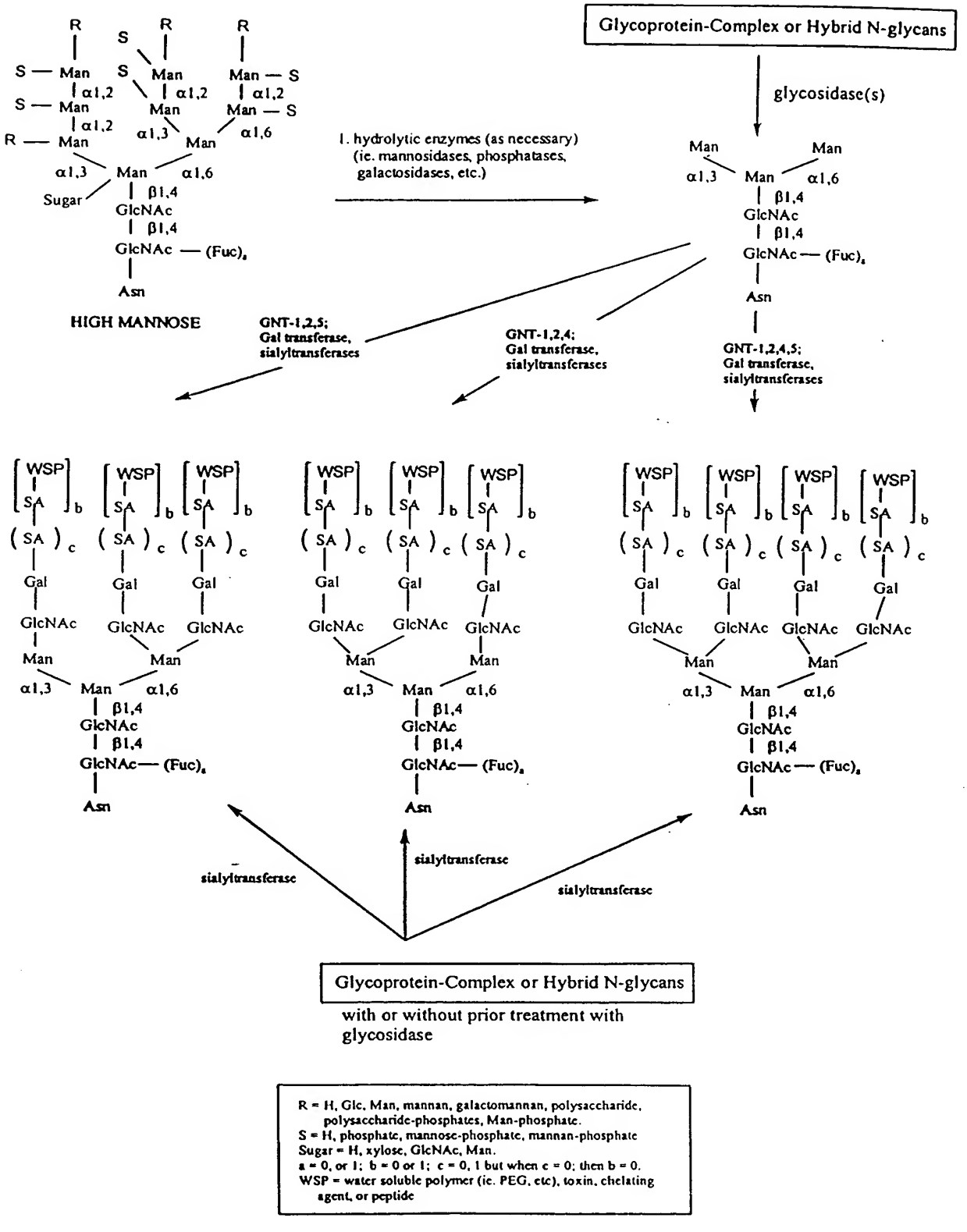


FIG. 7

Scheme 8.

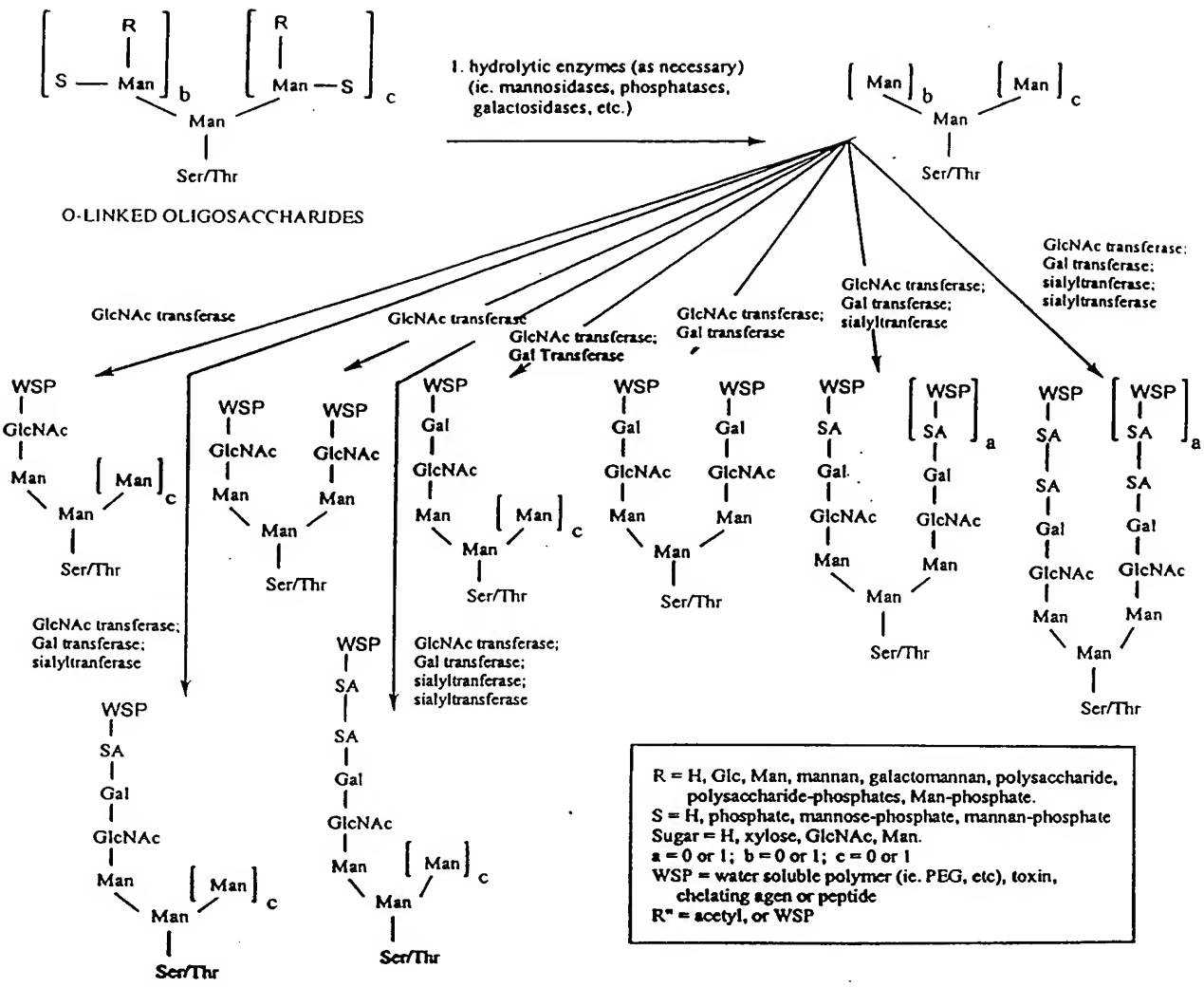


FIG. 8

Scheme 9.

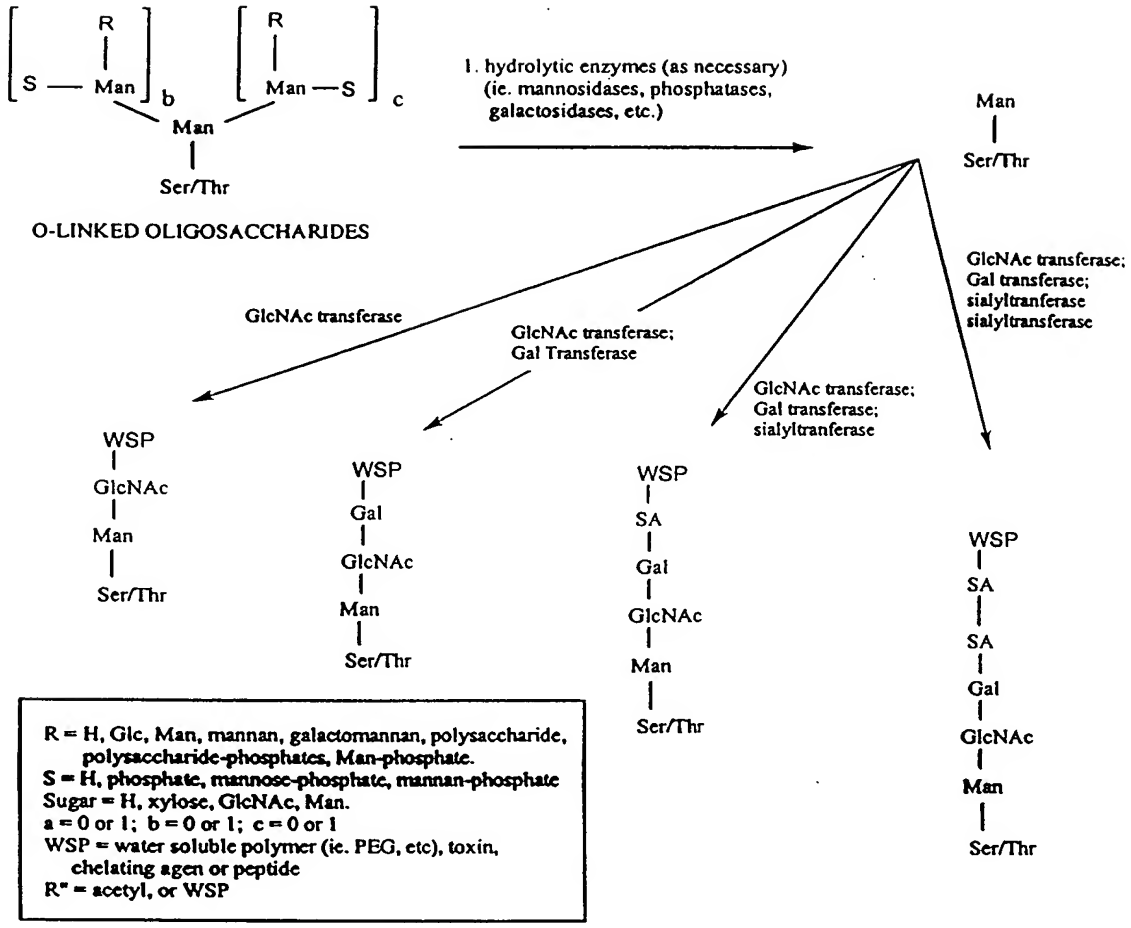
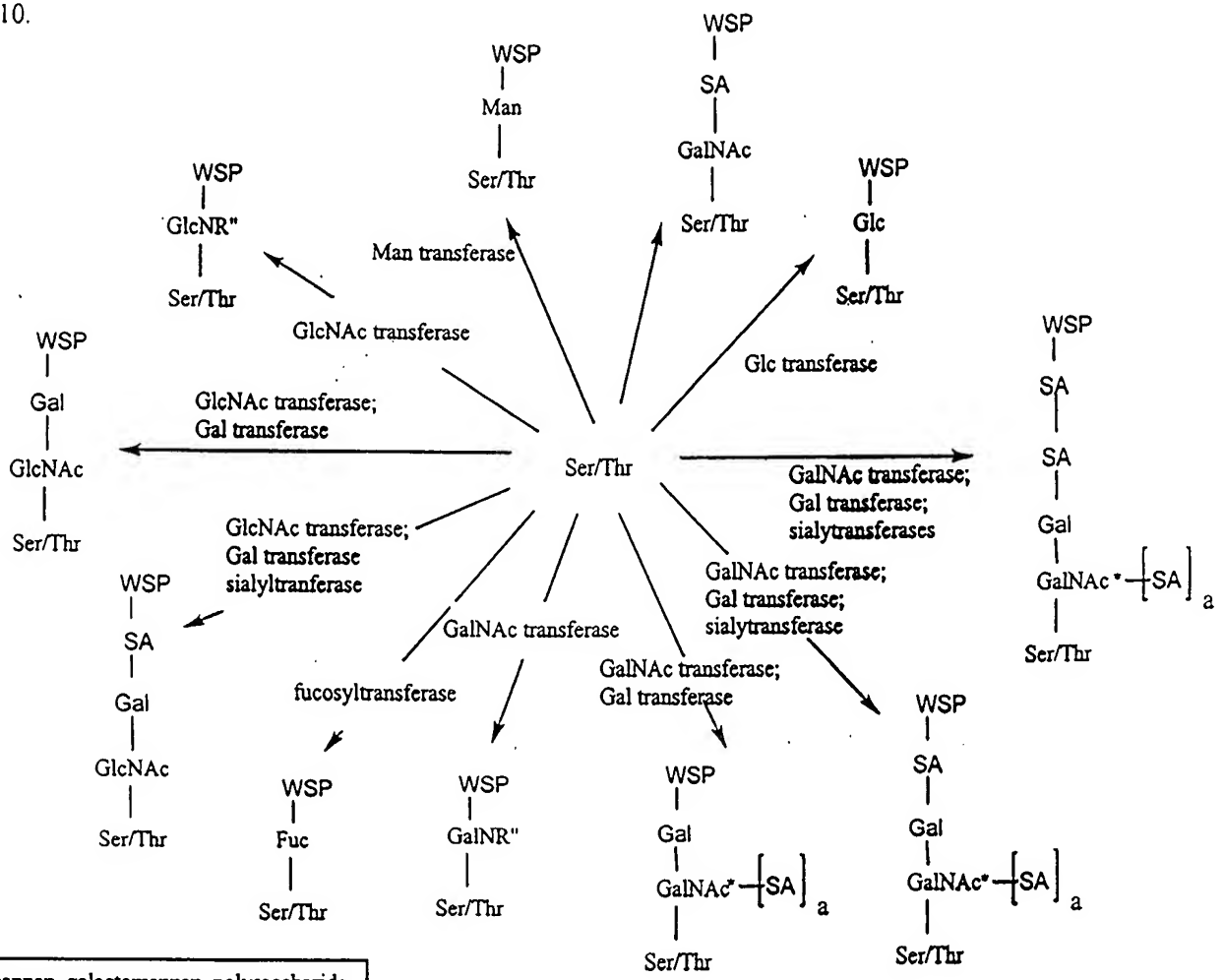


FIG. 9

Scheme 10.



R = H, Glc, Man, mannan, galactomannan, polysaccharide, polysaccharide-phosphates, Man-phosphate.
S = H, phosphate, mannose-phosphate, mannan-phosphate
Sugar = H, xylose, GlcNAc, Man.
a = 0 or 1; b = 0 or 1; c = 0 or 1
WSP = water soluble polymer (ie. PEG, etc), toxin, chelating agen or peptide
R" = acetyl, or WSP

FIG. 10

Toxin Name/ Source/ Alternate ID	CAS RN / Analogs	Indication/ Toxicity	Mechanism	Activity (IC50 nM); Tumor Type
		Chemical Structure		
SW-163E/ *Streptomyces* sp SNA 15896/ SW-163E	260794-24-9; 260794-25-0/ SW-163C; SW-163A; SW-163B	Cancer and Antibacterial/ low toxicity (mice ip)	not reported	0.3 P388 0.2 A2780 0.4 KB 1.6 colon 1.3 HL-60
		Chemical Structure		
Thiocoraline/ *Micromonospora marina* (actinomycete)	173046-02-1	Breast Cancer; Melanoma; Non-small lung cancer / not reported	DNA Polymerase alpha inhibitor (blocks cell progression from G1 to S)	lung, colon, CNS melanoma
		Chemical Structure		
Trunkamide A[1]/ *Lissoclinum* sp (aascidian)	181758-83-8	Cancer/ not reported	not reported	cell culture (IC50 in micrograms/mL); 0.5 P388; 0.5 A549;

FIG. 11A

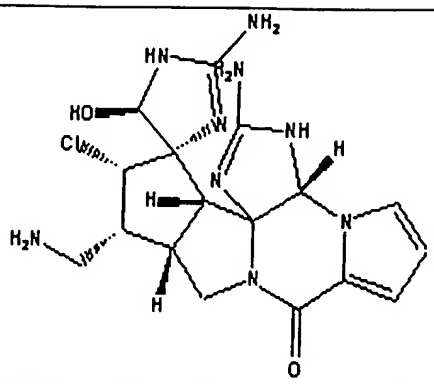
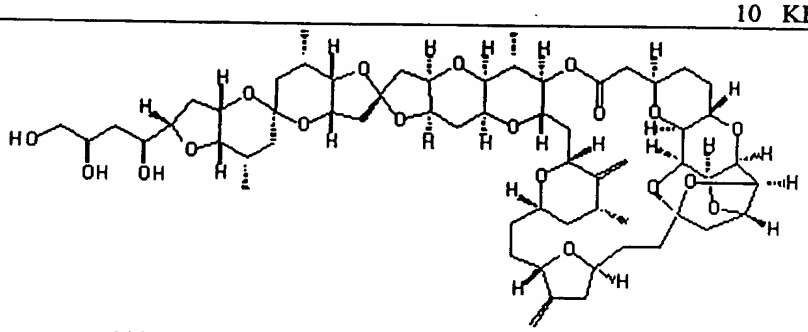
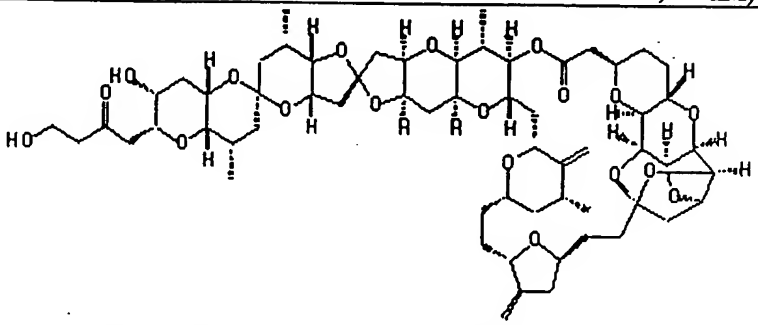
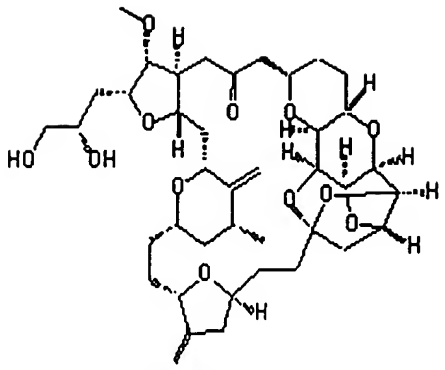
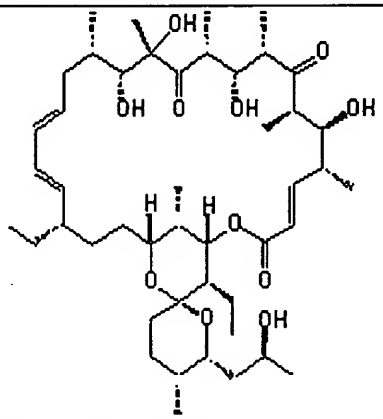
				0.5 HT-29; 1.0 MEL-28
 **Palauamine**[2]/ *Stylotella agminata* (sponge)	148717-58-2	Lung cancer/ LD50 (i.p. in mice) is 13 mg/Kg	not reported	cell culture (IC50 in micrograms/mL); 0.1 P388 0.2 A549 (lung) 2 HT-29 (colon) 10 KB
 **Halichondrin B**/ *Halichondria Okadai, Axinell Carteri and Phankell carteri* (sponges)/ NSC-609385	103614-76-2/ isohomohalic hondrin B	cancer/ myelotoxicity dose limiting (dogs, rats)	antitubulin; cell cycle inhibitor (inhibits GTP binding to tubulin)	NCI tumor panel; GI(50) from 50 nM to 0.1 nM; LC50's from 40 μM to 0.1 nM (many 0.1 to 25 nM)
 **Isohomo-halichondrin B**/ *Halichondria Okadai, Axinell Carteri and Phankell carteri* (sponges)/ NSC-650467	157078-48-3/ halichondrin B	melanoma, lung, CNS, colon, ovary/ not reported	antitubulin; cell cycle inhibitor (inhibits GTP binding to tubulin)	IC50's in 0.1 nM range (NCI tumor panel)

FIG. 11B



Halichondrin B analogs/ semi-synthetic starting from *Halichondria Okadai, Axinell Carteri and Phankell carteri* (sponges)/ ER-076349; ER-086526; B-1793; E-7389	253128-15-3/ ER-076349; ER-086526; B-1793; E-7389	solid tumors/ not reported	tubulin binding agent; disruption of mitotic spindles	cell culture (not reported); animal models active (tumor regression observed) in lymphoma, colon (multi-drug resistant).



NK-130119/ *Streptomyces bottropensis*/ NK-130119	132707-68-7	antifungal and anticancer/ not reported	not reported	25 ng/mL colon 8.5 ng/mL lung

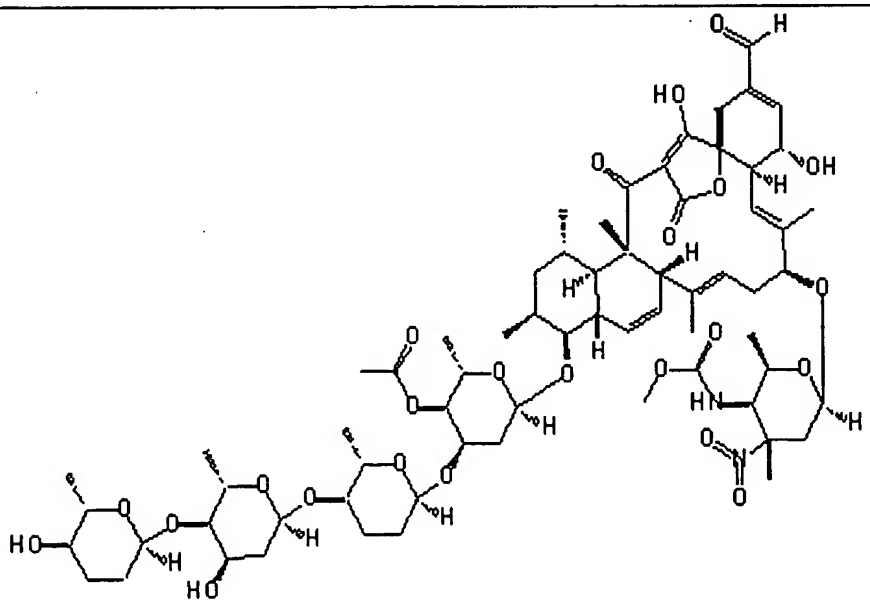


FIG. 11C

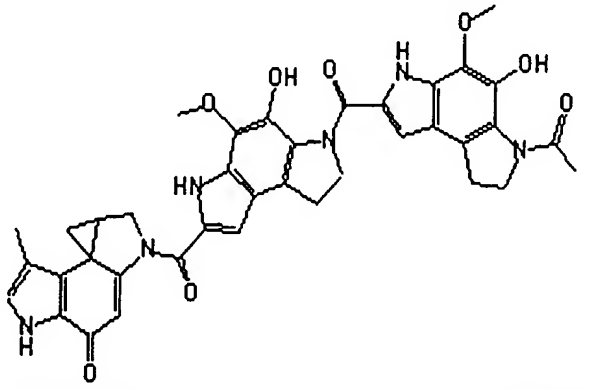
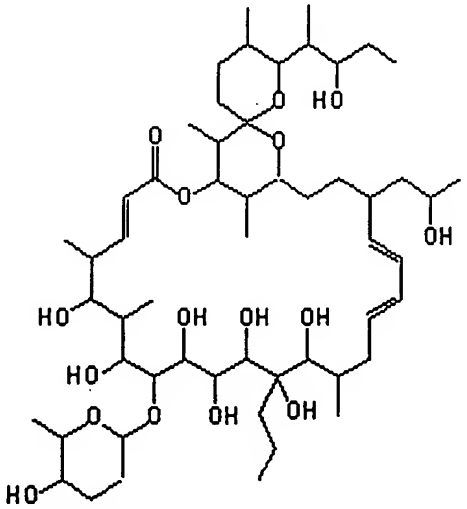
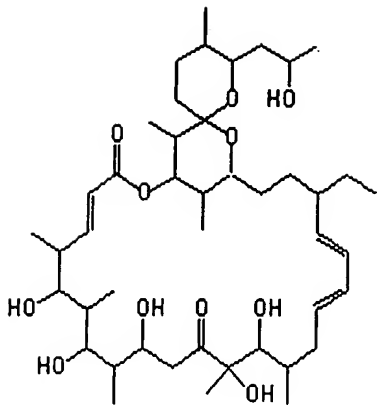
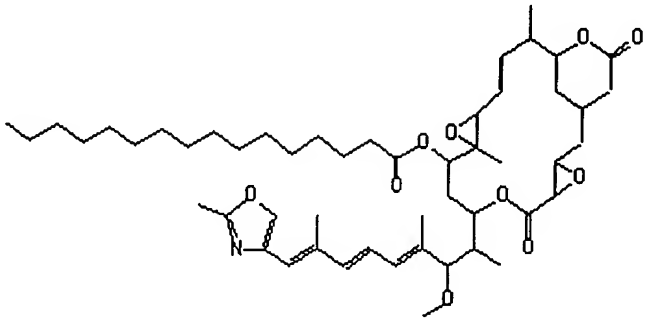
Tetrocarcin A/ not reported/ KF-67544	73666-84-9/ analogs are reported	cancer/ not reported	inhibits the anti- apoptotic functino of Bcl2	not reported
				
Gilvusmycin/ *Streptomyces* QM16	195052-09-6	cancer/ not reported	not reported	IC50's in ng/mL: 0.08 P388 0.86 K562 (CML) 0.72 A431 (EC) 0.75 MKN28 (GI); (for all < 1 nM)
				
IB-96212/ marine actinomycete/ IB-96212	220858-11-7/ IB-96212; IB-98214; IB-97227	Cancer and Antibacterial/ not reported	not reported	IC50's in ng/mL: 0.1 P388

FIG. 11D



BE-56384[3]/ *Streptomyces* Sp./ BE-56384	207570-04-5	cancer/ not reported	not reported	IC50's in ng/mL: 0.1 P388 0.29 colon 26 34 DLD-1 0.12 PC-13 0.12 MKM-45



Palmitoylrhizoxin/ semi-synthetic; *Rhizopus chinensis*	135819-69-1/ Analog of rhizoxin	cancer/ binds LDL; less cytotoxic than rhizoxin	tubulin binding agent (cell cycle inhibitor)	not reported

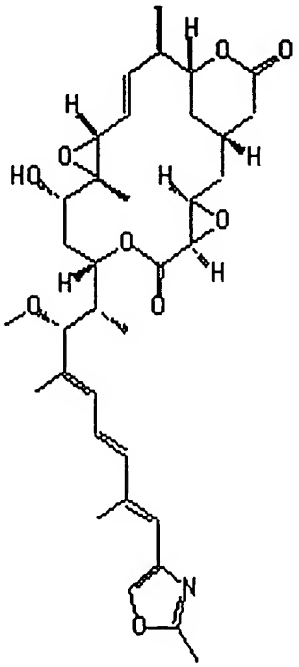


FIG. 11E

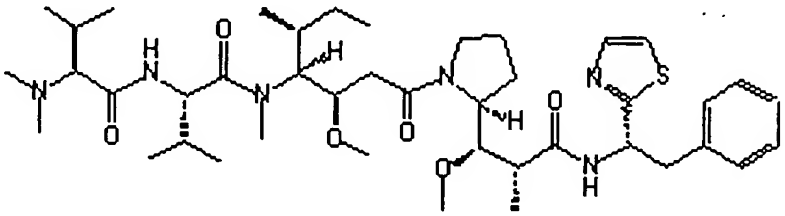
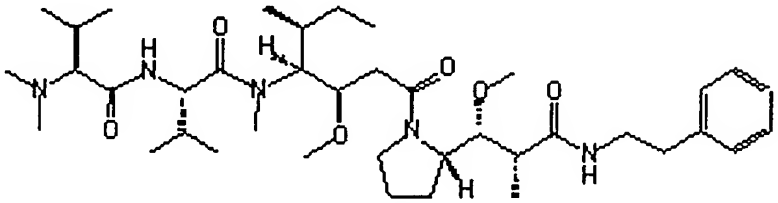
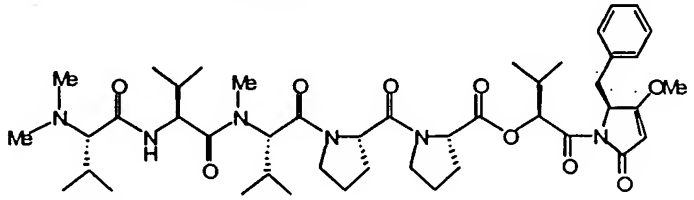
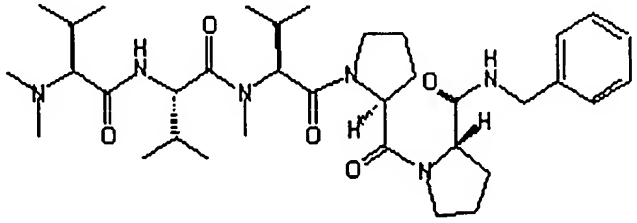
Rhizoxin/ *Rhizopus chinensis*/ WF-1360; NSC-332598; FR-900216	95917-95-6; 90996-54-6	melanoma, lung, CNS, colon, ovary, renal, breast, head and neck/ Rapid Drug clearance; High AUC correlates with high toxicity	tubulin binding agent (cell cycle inhibitor)	NCI tumor panel (NSC 332598); log GI50's: 50 nM to 50 fM; log LC50's: 50 μM to 0.5 nM (several cell lines at 50 fM).
				
Dolastatin-10/ *Dolabella auricularia* (sea hare)/ NSC-376128	110417-88-4/ other Dolistatins (ie. 15) and analogs	prostate, melanoma, leukemia/ myelotoxicity (at greater than 0.3 pM)	tubulin binding (tubulin aggregation)	NCI tumor panel (60 cell line; GI50); 25 nM to 1 pM (most < 1 nM) (three cell lines μM)
				
soblidotin/ synthetic/ TZT-1027; auristatin PE	149606-27-9/ analogs prepared	cancer (pancreas, esophageal colon, breast, lung, etc) / MTD was 1.8 mg/Kg (IV); toxicity not reported	tubulin binding agent	cell culture: colon, melanoma, M5076 tumors, P388 with 75-85% inhibition (dose not reported)
				
Dolastatin-15/ *Dolabella auricularia* (sea hare)	not reported/ other Dolistatins (ie. 15) and analogs	cancer/ not reported	Tubulin binding (tubuline aggregation)	NCI tumor panel (60 cell line; GI50); 25 nM to 39 pM (most < 1 nM) (one cell line 2.5 μM); most active in breast
				
Cemadotin[4]/	1159776-69-	melanoma/	tubulin	NCI tumor panel (NCS

FIG. 11F

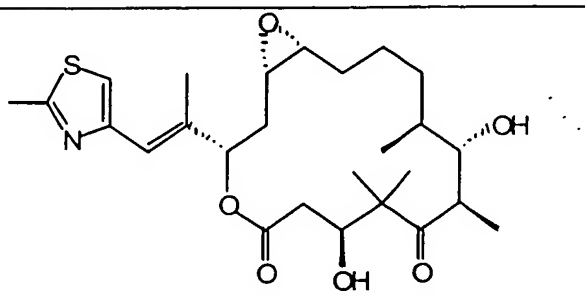
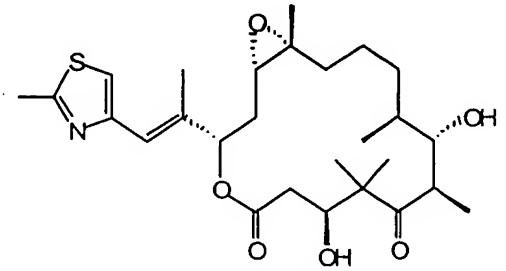
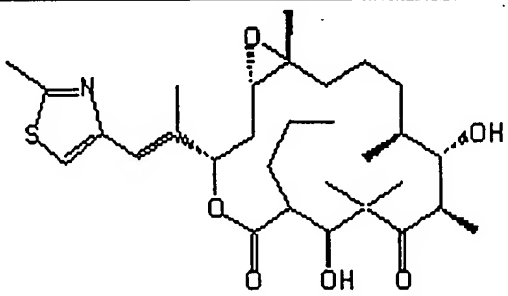
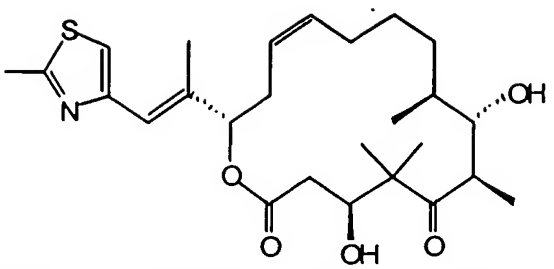
Synthetic; Parent Dolastatin-15 was isolated from *Dolabella auricularia* (sea hare)/ LU-103793; NSC D-669356	9/ many analogs	hypertension, myocardial ischemia and myelosuppression were dose-limiting toxicities.	binding (tubulin aggregation)	D-669356); active in breast, ovary, endometrial, sarcomas and drug resistant cell lines. Data not public.
				
Epothilone A/ Synthetic or isolated from *Sorangium cellulosum* (myxococcales) strain So ce90)	not reported/ many analogs	cancer/ not reported	tubulin binding (tubulin polymeriza-tion)	IC50's of; 1.5 nM MCF-7 (breast) 27.1 nM MCF-7/ADR 2.1 nM KB-31 (melanoma) 3.2 nM HCT-116
				
Epothilone B/ Synthetic or isolated from *Sorangium cellulosum* (myxococcales) strain So ce90) / EPO-906	152044054-7/ many analogs	Solid tumors (breast, ovarian, etc)/ well tolerated; t1/2 of 2.5 hrs; partial responses (phase I); diarrhea major side effect.	tubulin binding (tubulin polymeriza-tion)	IC50's of; 0.18 nM MCF-7 (breast) 2.92 nM MCF-7/ADR 0.19 nM KB-31 (melanoma) 0.42 nM HCT-116; broad activity reported
				
Epothilone Analog / Synthetic or semi-synthetic; Original lead, Epothilone A, isolated from *Sorangium cellulosum* (myxococcales) strain So ce90)/ ZK-EPO	not reported / hundreds of analogs	cancer/ not reported	tubulin binding (tubulin polymeriza-tion)	IC50's of 0.30 to 1.80 nM in various tumor cell lines; active in drug resistant cell lines

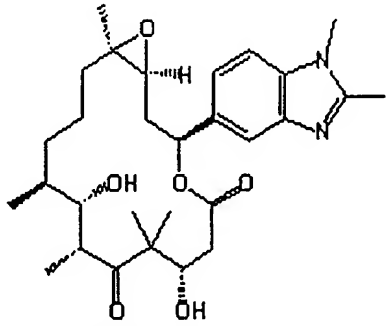
FIG. 11G



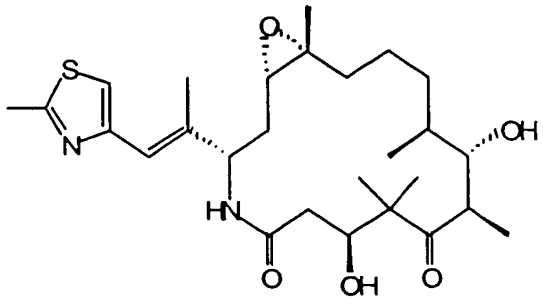
Epothilone D / Epothilone D, isolated from *Sorangium cellulosum* (myxococcales) strain So ce90)/ KOS-862	189452-10-9/ many analogs	Solid tumors (breast, ovarian, etc)/ emesis and anemia; t1/2 of 5-10 hrs.	tubulin binding (tubulin polymeriza-tion)	NCI tumor panel (NSC-703147; IC50); 0.19 nM KB-31 (melanoma) 0.42 nM HCT-116; broad activity reported

Structure Not Identified

Epothilone D analog [5]/ Synthetic or semi-synthetic; Original lead, Epothilone D, isolated from *Sorangium cellulosum* (myxococcales) strain So ce90)/ KOS-166-24	189453-10-9/ hundreds of analogs	Solid tumors; not reported	tubulin binding (tubulin polymeriza-tion)	not reported



Epothilone Analog / Synthetic; Original lead, Epothilone A, isolated from *Sorangium cellulosum* (myxococcales) strain So ce90)/ CGP-85715	not reported/ hundreds of analogs	cancer; not reported	tubulin binding (tubulin polymeriza-tion)	not reported



Epothilone Analog/	219989-84-1/	non-small cell Lung,	tubulin	NCI tumor Panel (NSC-

FIG. 11H

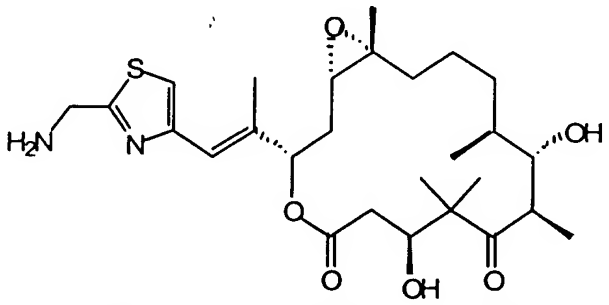
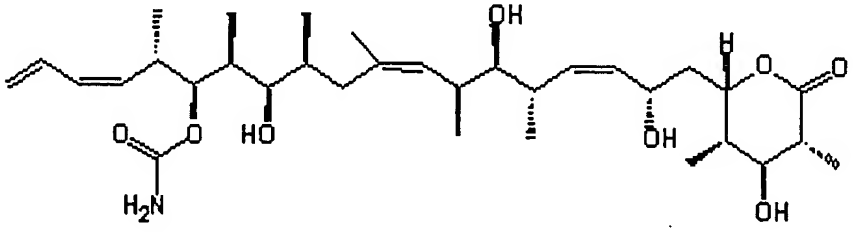
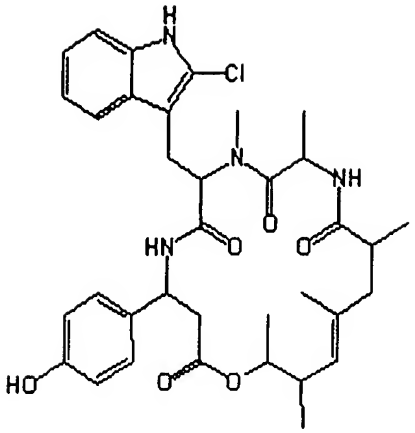
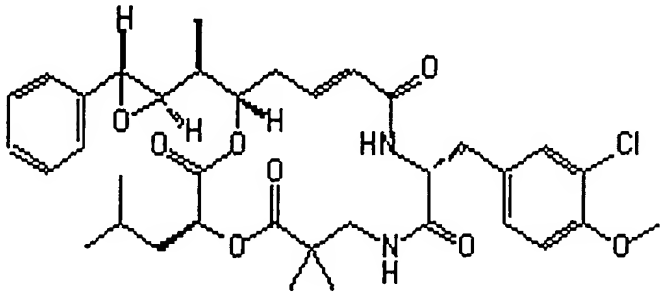
Synthetic or semi-synthetic; Original lead, Epothilone B, isolated from *Sorangium cellulosum* (myxococcales) strain So ce90)/ BMS-247550	hundreds of analogs	breast, stomach tumor (objective responses in breast ovarian and lung)/ sever toxicity (fatigue, anorexia, nauseas, vomiting, neuropathy myalgia)	binding (tubulin polymerizati on)	710428 & NSC-710468); 8-32 nM (NCI data not available)
				
Epothilone Analog / Synthetic or semi-synthetic; Original lead, Epothilone B, isolated from *Sorangium cellulosum* (myxococcales) strain So ce90)/ BMS-310705	not reported/ hundreds of analogs	advanced cancers/ adverse events (diarrhea, nausea, vomiting , fatigue, neutropenia); t1/2 of 3.5 hrs; improved water solubility to BMS 247550.	tubulin binding (tubulin polymeriza-tion)	broad activity with IC50's of 0.7 to 10 nM
				
Discodermolide / synthetic; orginally isolated from *Discodermia dissoluta* (deep water sponge); rare compound (7 mg per 0.5 Kg sponge/ XAA-296	127943-53-7/ analogs less potent	solid tumors/ not reported; 100-fold increase in water solubility over taxol	tubulin stabilizing agent (similar to taxol)	Broad activity (A549-nsclung, prostate, P388, ovarian with IC50's about 10 nM) including multi-drug resistant cell lines;

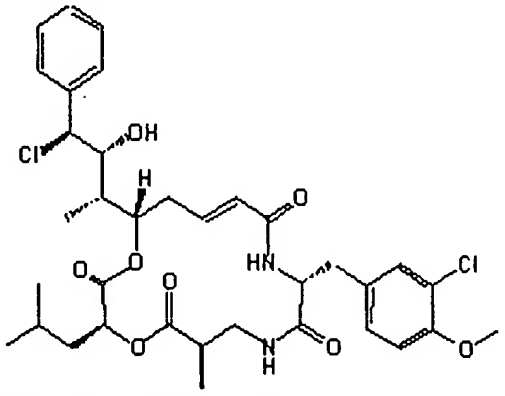
FIG. 11I



Chondramide D/ not reported	172430-63-6	cancer/ not reported	tubulin binding agent; actin polymeriza-tion inhibitor	5 nM A-549 (epidermoid carcinoma) 15 nM A-498 (kidney) 14 nM A549 (lung) 5 nM SK-OV-3 (ovary) 3 nM U-937 (lymphoma)



Cryptophycin analogs (including 52, 55 and others)[6]/ *Nostoc* sp GSV 224 (blue-green algae) isolated Cryptophycin 1./ LY-355703; Ly-355702; NSC-667642	204990-60-3 and 186256-67-7/ many potent analogs prepared at Lilly	solid tumors, colon cancer/ Phase II studies halted because of severe toxicity with one death resulting from drug;	tubulin polymeriza-tion inhibitor	broad activity (lung, breast, colon, leukemia) with IC50's of 2 to 40 pM; active against multi-drug resistance cell lines (resistant to MDR pump). NCI tumor panel, GI50's from 100 nM to 10 pM; LC50's from 100 nM to 25 pM.



Cryptophycin 8/	168482-36-8;	solid tumors/	tubulin	broad spectrum

FIG. 11J

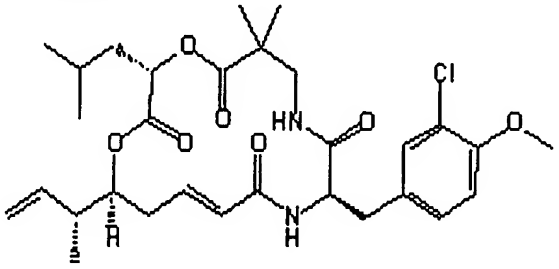
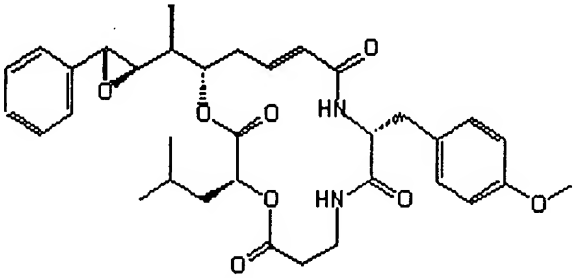
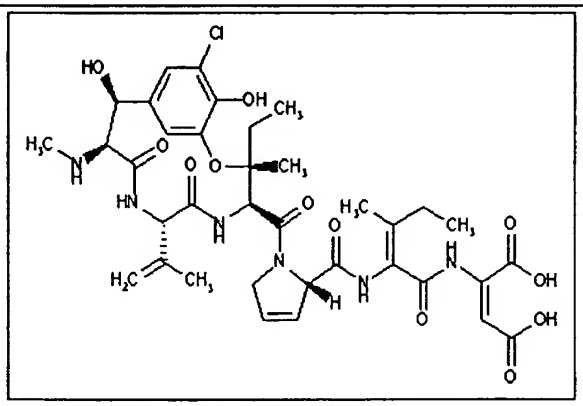
semi-synthetic; starting material from *Nostoc* sp.	168482-40-4; 18665-94-1; 124689-65-2; 125546-14-7/ cryptophycin 5, 15 and 35	not reported	polymeriza-tion inhibitor	anticancer activity (cell culture) including multi-drug resistant tumors
Cryptophycin analogs[7]/ synthetic; semi-synthetic, starting material from *Nostoc* sp./ LY-404291	 219660-54-5/ LY-404292	solid tumors/ not reported	topoisomer-ase inhibitors	not reported
Arenastatin A analogs[8]/ *Dysidea arenaria* (marine sponge)/ Cryptophycin B; NSC-670038	 not reported/ analogs prepared	cancer/ not reported	inhibits tubulin polymeriza-tion	8.7 nM (5 pg/mL) KB (nasopharyngeal); NCI tumor panel (GI50's); 100 pM to 3 pM
Phomopsin A/ *Diaporte toxicus* or *Phomopsin leptostromiformis* (fungi)	 not reported	Liver cancer (not as potent in other cancers)/ not reported	tubulin binding agent	potent anticancer activity especially against liver cancer

FIG. 11K

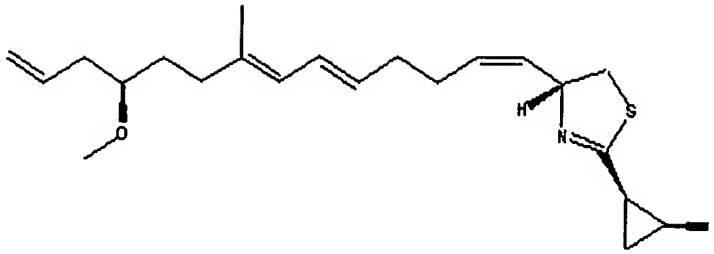
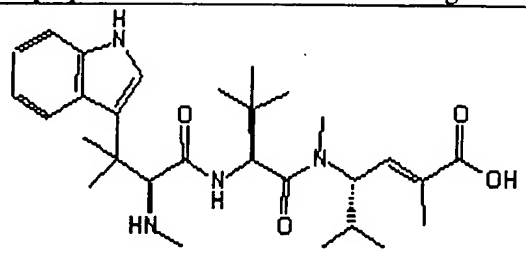
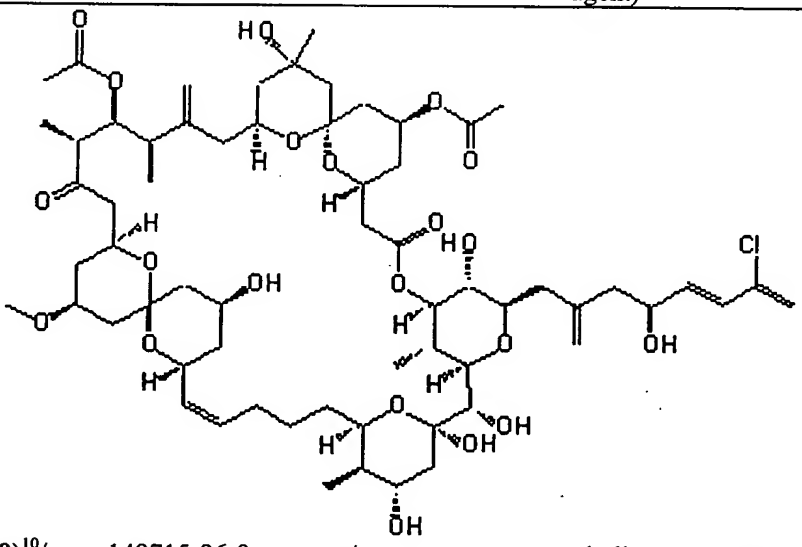
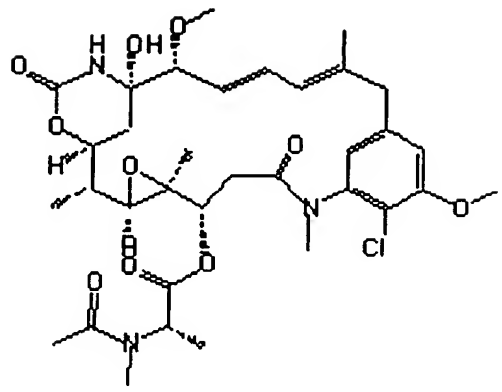
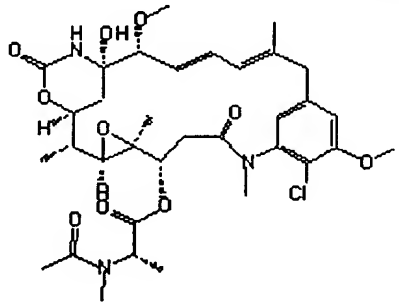
				
Curacin A and analogs/ *Lyngbya majuscula* (blue green cyanobacterium)	155233-30-0/ analogs have been prepared	Cancer/ not reported	Tubulin binding agent	broad activity (cancer cell lines); 1-29 nM
				
Hemiasterlins A & B and analogs[9]/ *Cymbastela* sp.	not reported/ criamide A & B; geodiamiolid-G	Cancer/ not reported	Antimitotic agent (tubulin binding agent)	broad activity: 0.3-3 nM MCF7 (breast); 0.4 ng/mL P388
				
Spongistatins (1-9)[10]/ *Spirastrell spinispirulifera* (sea sponge)	149715-96-8; 158734-18-0; 158681-42-6; 158080-65-0; 150642-07-2; 153698-80-7; 153745-94-9; 150624-44-5; 158734-19-1/ other spongistatins	cancer/ not reported	tubulin binding agent	Most potent compounds ever tested in NCI panel cell line (mean GI50's of 0.1 nM; Spongistatin-1 GI50's of 0.025-0.035 nM with extremely potent activity against a subset of highly chemoresistant tumor types

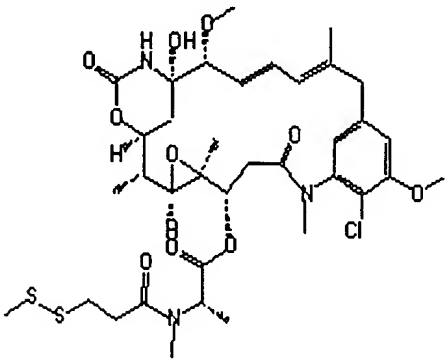
FIG. 11L



Maytansine/ *Maytenus* sp./ NSC-153858	35846-53-8/ other related macrolides	cancer/ severe toxicity	tubulin binding agent (causes extensive disassembly of the microtubule and totally prevents tubulin spiralizaiton)	Broad Activity in NCI tumor panel (NSC-153858; NSC-153858); NCI tumor panel, GI50's from 3 μM to 0.1 pM; LC50's from 250 μM to 10 pM. Two different experiments gave very different potencies.



Maytansine-IgG(EGFR directed)-conjugate[11]/ semi-synthetic; starting material from *Maytenus* sp.	not reported/ other related macrolides	breast , head and neck, Squamous cell carcinoma/ not reported	EGFR binding and tubulin binding	not reported



Maytansine-IgG(CD56 antigen)-conjugate[12], 3.5 drug molecules per IgG/ semi-synthetic; starting material from *Maytenus*	not reported/ other related macrolides	Neuroendocrine, small-cell lung, carcinoma/ mild toxicity (fatigue, nausea, headaches and mild peripheral	CD56 binding and tubulin binding	antigen-specific cytotoxicity (cell culture; epidermal, breast, renal ovarian colon) with IC50's of

FIG. 11M

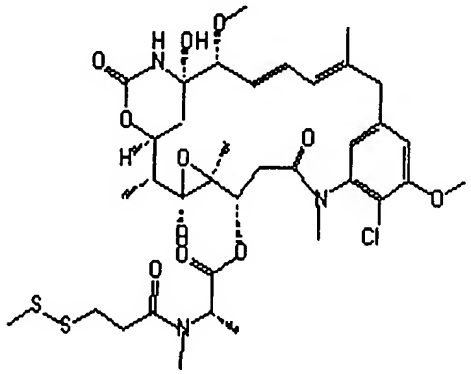
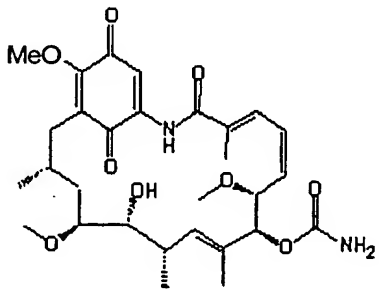
sp./ huN901-DM1		neuropathy); no hematological toxicity; MTD 60 mg/Kg, I.V., weekly for 4 weeks; only stable disease reported (humans)		10-40 pM; animal studies (miceSCLC tumor--alone and in combination with taxol or cisplatin completely eliminated tumors).
				
Maytansine-IgG(CEA antigen)-conjugate[13], 4 drug molecules per IgG/ semi-synthetic; starting material from *Maytenus* sp./ C424-DM1	not reported/ other related macrolides	non-small-cell lung, carcinoma pancreas, lung, colon/ mild toxicity (fatigue, nausea, headaches and mild peripheral neuropathy); pancreatic lipase elevated; MTD 88 mg/Kg, I.V., every 21 days; only stable disease reported (humans); t1/2 was 44 hr.	CEA binding and tubulin binding	antigen-specific cytotoxicity (cell culture; epidermal, breast, renal ovarian colon) with IC50's of 10-40 pM; animal studies (mice: melanoma [COLO-205]--alone and in combination with taxol or cisplatin completely eliminated tumors);
				
Geldanamycin / *Streptomyces hygroscopicus* var. Geldanus/ NSC-212518; Antibiotic U 29135; NSC-122750	30562-34-6/ natural derivatives	cancer/ not reported	binds Hsp 90 chaperone and inhibits function	NCI tumor panel (cell culture); 5.3 to 100 nM; most active in colon, lung and leukemia. NCI tumor panel, GI50's from 10 μM to 0.1 nM; LC50's from 100 μM to 100 nM. Two assays with very different potencies.

FIG. 11N

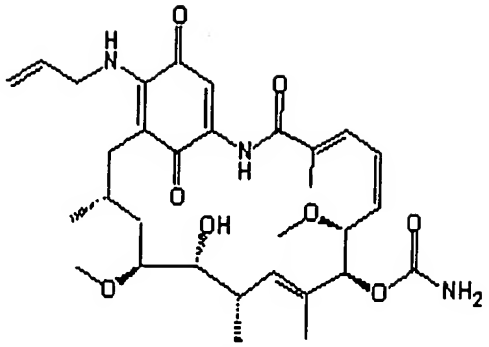
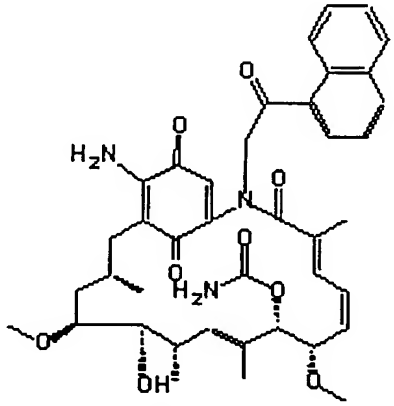
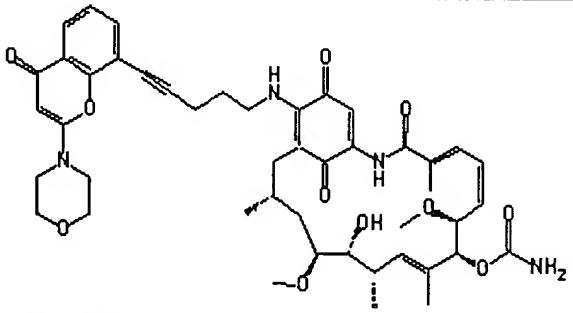
				
Geldanamycin Analog/ semi-synthetic; / CP-127374; 17-AAG; NSC-330507	745747-14-7/ Kosan, NCI and UK looking for analogs with longer t1/2 and oral activity; analogs include: NSC-255110; 682300; 683661; 683663.	solid tumors/ Dose limiting toxicities (anemia, anorexia, diarrhea, nausea and vomiting); t1/2 (i.v.) is about 90 min; no objective responses measured at 88 mg/Kg (i.v. daily for 5 days, every 21 days);	binds Hsp 90 chaperone and inhibits function	cell culture (not reported); animal models active (tumor regression observed) in breast, ovary, melanoma, colon.
				
Geldanamycin analog/ semi-synthetic; / CP-202567	not reported/ analogs prepared	solid tumors/ not reported	binds Hsp 90 chaperone and inhibits function	not reported
				
Geldanamycin conjugates/ semi-synthetic; / LY-294002-GM; PI3K-1-GM	345232-44-2/ analogs prepared	breast/ not reported	binds Hsp 90 chaperone and inhibits function; binds and	cell culture (no reported); animal models performed

FIG. 11O

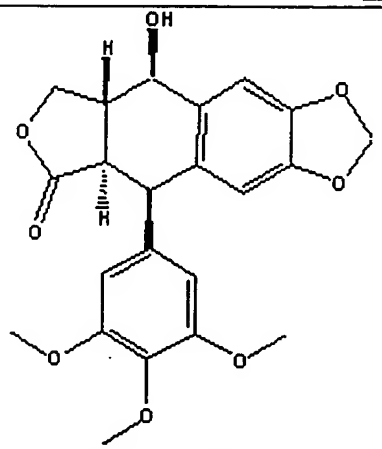
			inhibits PI-3 kinase	
Structure Not Reported				
Geldanamycin Analog/ not reported/ CNF-101	not reported/ analogs prepared	breast, prostate/ not reported	binds Hsp 90 chaperone and inhibits function	not reported
Structure Not Reported				
Geldanamycin-testosterone conjugate/ semi-synthetic/ GMT-1	not reported/ analogs prepared	prostate/ not reported	binds Hsp 90 chaperone and inhibits function and testosterone receptors where it is internalized	not reported; conjugate has a 15-fold selective cytotoxicity for androgen positive prostate cells
				
Podophyllotoxin/ *Podophyllum* sp.	518-28-5/ many analogs	Verruca vulgaris, Condyloma/ severe toxicity when given i.v. or s.c.	tubulin inhibitor and topoisomer-ase inhibitor	broad activity (cell culture) with IC50's in μM range

FIG. 11P

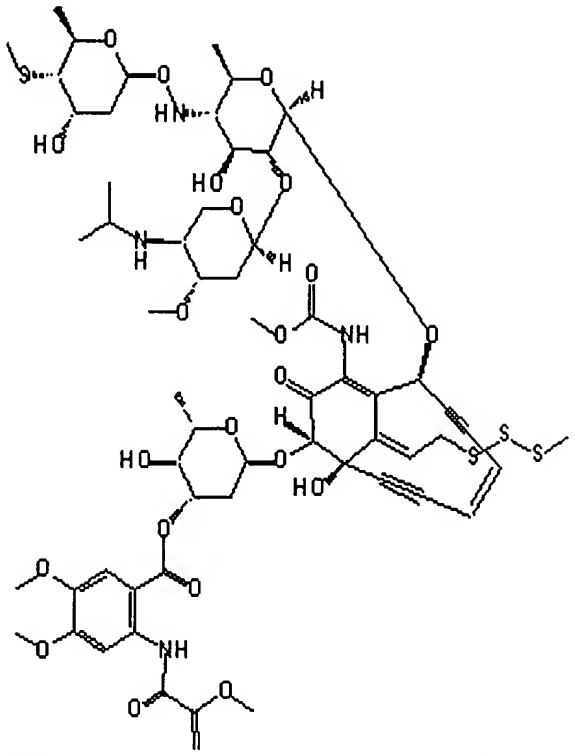
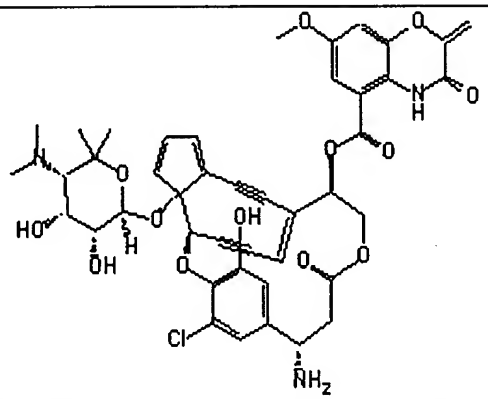
				
esperamicin-A1/ not known/ BBM-1675A1; BMY-28175; GGM-1675	99674-26-7	cancer/ not reported (suspected severe toxicity)	DNA cleaving agent	highly potent activity (cell culture); animal models highly potent with optimal dose of 0.16 micrograms/Kg
				
C-1027[14]/ *Streptomyces setonii* C-1027/ C-1027	120177-69-7	cancer (examined hepatoma, breast, lung and leukemia/ not reported	DNA cleaving agent	extremely potent (cell culture) IC50's in pM and fM; conjugated to antibodies the potency remains the same (ie. 5.5 to 42 pM);

FIG. 11Q

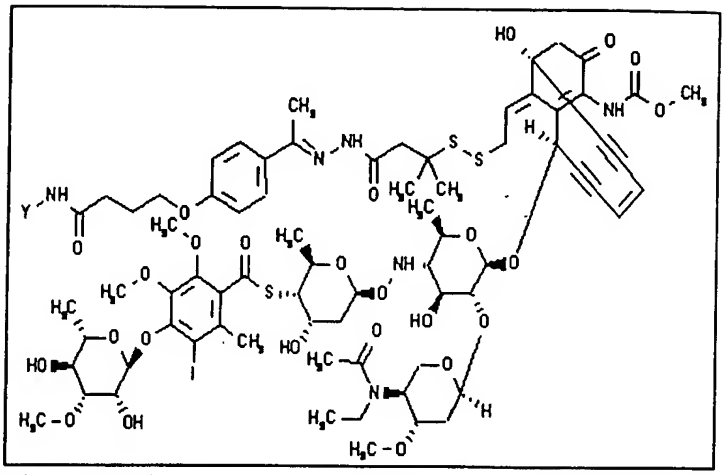
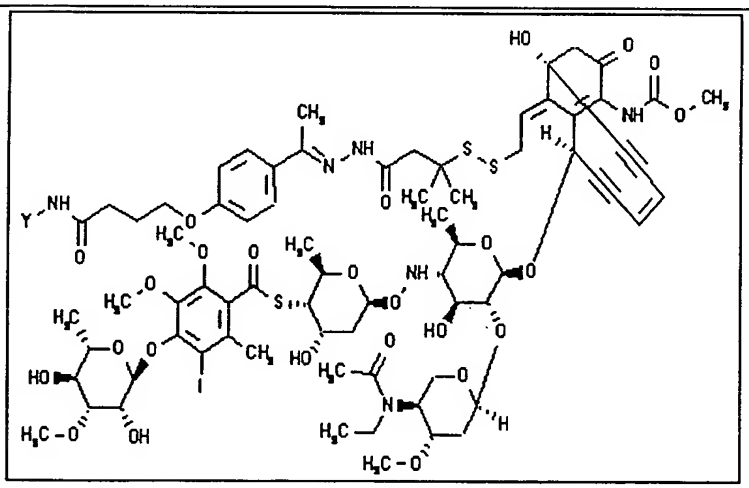
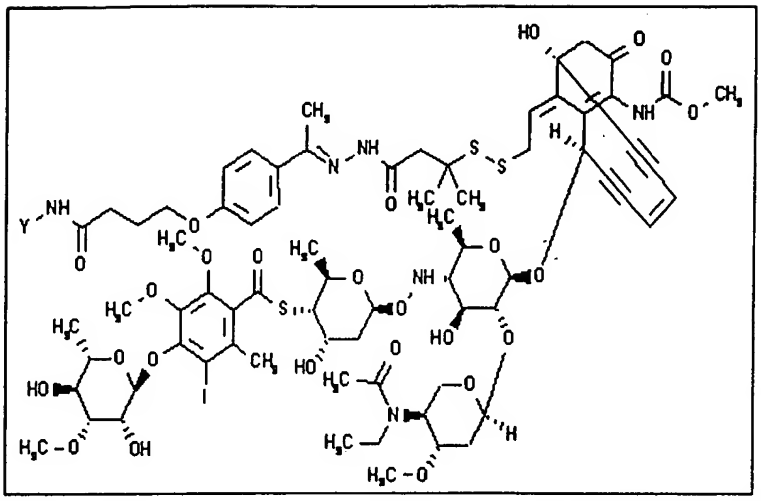
Pr(-X-S-S-W)$_m$ m = 0.5 - 15 Pr = proteinaceous carrier W = calicheamicin minus Me-S-S-S X = linker Y = antibody P76.6				
Calicheamicin-IgG(CD33 antigen)-conjugate[15]/ semi-synthetic: *Micromonospora echinospora*/ gemtuzumab ozogamicin; mylotarg; WAY-CMA-676; CMA-676; CDP-771	113440-58-7; 220578-59-6/ several reported in patents	AML/ mild toxicity	DNA cleaving agent	Kills CD33+ cells (HL-60, NOMO-1, and NKM-1) at 100 ng/mL; MDR cell lines are not effected by the drug.
Pr(-X-S-S-W)$_m$ m = 0.5 - 15 Pr = proteinaceous carrier W = calicheamicin minus Me-S-S-S X = linker Y = antibody P76.6				
Calicheamicin-IgG-conjugates[16]/ semi-synthetic: *Micromonospora echinospora*	113440-58-7; 220578-59-6	cancer/ not reported	DNA cleaving agent	TBD

FIG. 11R

Calicheamicin-IgG(OBA1 antigen) conjugate/ semi-synthetic: *Micromonospora echinospora/* OBA1-H8	not reported	cancer/ not reported	DNA cleaving agent	all human cancer; data not reported

$Pr(-X-S-S-W)_m$

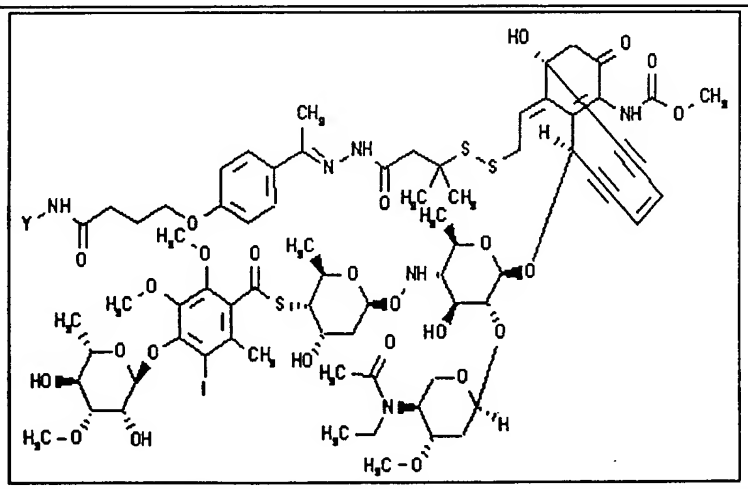
m = 0.5 - 15
Pr = proteinaceous carrier
W = calicheamicin minus Me-S-S-S
X = linker
Y = antibody P76.6



Calicheamicin-IgG(CD22 antigen) conjugate/ semi-synthetic: *Micromonospora echinospora/* CMC-544	not reported	non-Hodgkin lymphoma, cancer/ not reported	DNA cleaving agent	all human cancer; data not reported

$Pr(-X-S-S-W)_m$

m = 0.5 - 15
Pr = proteinaceous carrier
W = calicheamicin minus Me-S-S-S
X = linker
Y = antibody P76.6



parially esterified polystyrene maleic acid copolymer (SMA) conjugated to neocarzinostatin (NCS)

Neocarzinostatin[17]/ semi-synthetic; *Streptomyces carconistaticus/* Zinostatin stimalamer; YM-881; YM-16881	123760-07-6; 9014-02-2	liver cancer and brain cancer/ not reported	DNA cleaving agent	cell culture data not reported.

FIG. 11S

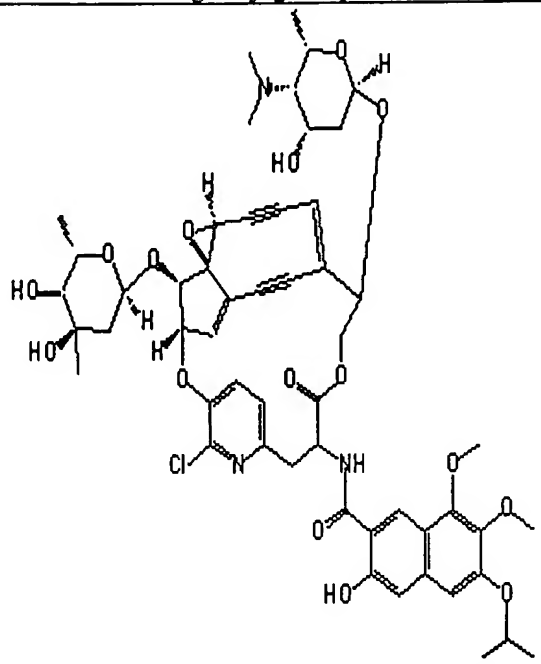
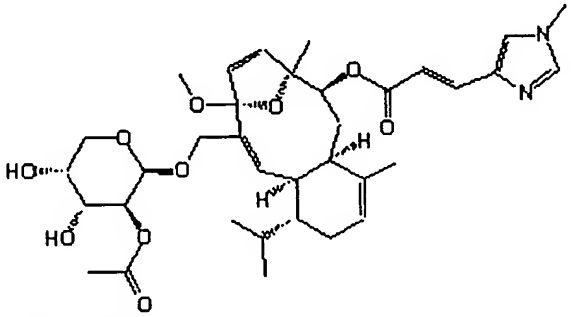
IgG (TES-23)-conjugated to neocarzinostatin				
Neocarzinostatin/ not reported/ TES-23-NCS	not reported	solid tumors/ toxicity not reported; the TES-23 antibody (without anticancer agent) was as effective at eliminating tumors as the drug conjugated protein	DNA cleaving agent and immunostim-ulator	cell culture data not reported.
				
Kedarcidin[18]/ *Streptoalloteichus* sp NOV strain L5856, ATCC 53650/ NSC-646276	128512-40-3; 128512-39-0/ chromophore and protein conjugate	cancer/ not reported	DNA cleaving agent	cell culture (IC50's in ng/mL), 0.4 HCT116; 0.3 HCT116/VP35; 0.3 HCT116/VM46; 0.2 A2780; 1.3 A2780/DDP. animal models in P388 and B-16 melanoma. NCI tumor panel, GI50's from 50 μM to 5 μM.
				
Eleutherobins/ marine coral	174545-76-7/ sarcodictyins (marine coral)	cancer/ not reported	tubulin binding agent	similar potency to taxol; not effective against MDR cell lines

FIG. 11T

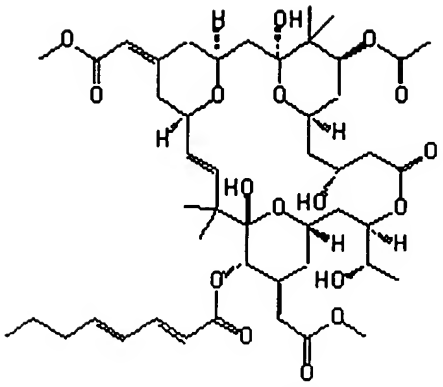
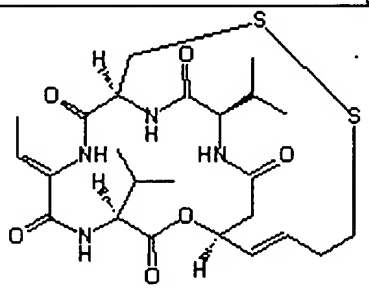
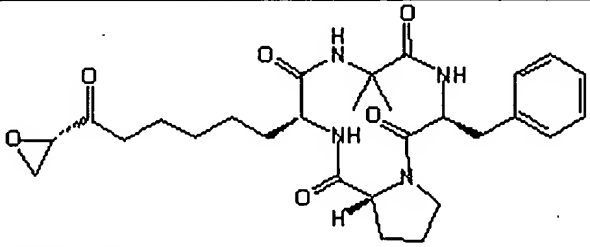
				
Bryostatin-1/ *Bugula neritina* (marine bryosoan)/ GMY-45618; NSC-339555	83314-01-6	leukemia, melanoma, lung, cancer/ myalgia; accumulated toxicity; poor water solubility; dose limiting toxicity	immunostim-ulant (TNF, GMCSF, etc); enhances cell kill by current anticancer agents	not reported
				
FR-901228/ *Chromobacterium violaceum* strain 968/ NSC-63-176; FK-228	128517-07-7	leukemia, T-cell lymphoma, cancer/ toxic doses (LD50) 6.4 and 10 mg/Kg, ip and iv respectively; GI toxicity, lymphoid atrophy; dose limiting toxicity (human) 18 mg/Kg; t1/2 of 8 hrs (human)	histone deacetylase inhiibitor	In vitro cell lines (NCI tumor panel); IC50's of between 0.56 and 4.1 nM (breast, lung, gastric colon, leukemia)
				
Chlamydocin/ not reported	53342-16-8	cancer/ not reported	histone deacetylase inhiibitor	not reported (cell culture); inhibits histone deacetylase at an IC50 of 1.3 nM

FIG. 11U

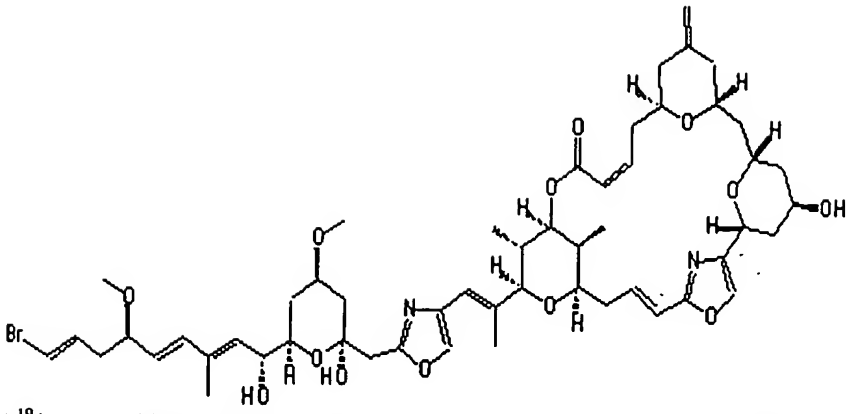
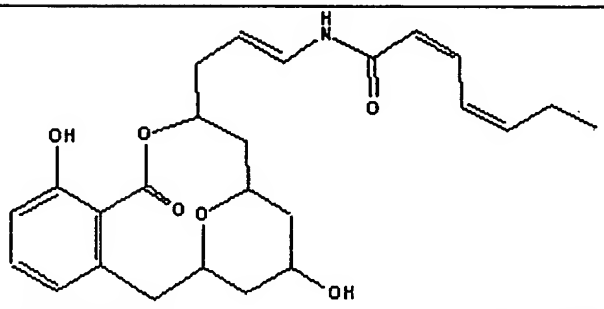
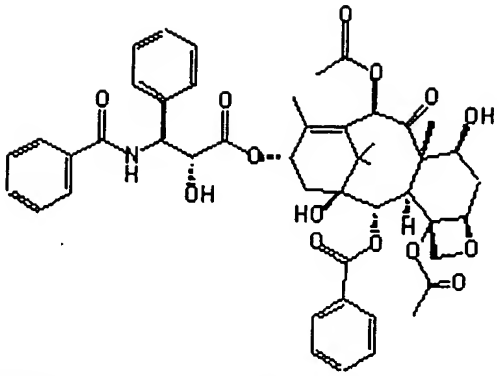
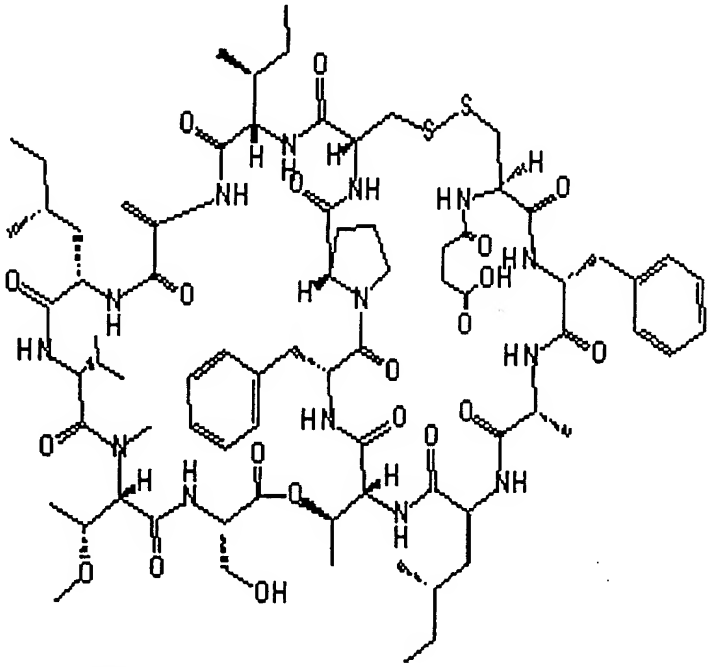
 **Phorboxazole A**[19]/ marine sponge	181377-57-1; 165689-31-6; 180911-82-4; 165883-76-1/ analogs prepared	leukemia, myeloma/ not reported	not reported (induces apoptosis)	NCI tumor panel (details not reported); IC50's of 1-10 nM. The inhibition values (clonogenic growth of human cancer cells) at 10 nM ranged from 6.2 to > 99.9% against NALM-6 human B-lineage acute lymophoblastic leukemia cells, BT-20 breast cancer cells and U373 glioblastoma cells, with the specified compound showing inhibition values in the range of 42.4 to > 99.9% against these cell lines.; IC50's are nM for MDR cell lines.
 **Apicularen A**/ *Chondromyces robustus*	220757-06-2/ natural derivatives	cancer/ not reported	not reported	IC50's of 0.1 to 3 ng/mL (KB-3-A, KB-Va, K562, HL60, U937, A498, A549, PV3 and SK-OV3)

FIG. 11V



Taxol/ Pacific yew and fungi/ Paclitaxel; NSC-125973	33069624/ many analogs	cancer; breast, prostate, ovary, colon, lung, head & neck, etc./ severe toxicity (grade III and IV)	tubulin binding agent	NCI tumor panel; GI50's of 3 nM to 1 μM; TGI 50 nM to 25 μM



Vitilevuamide/ *Didemnum cuculliferum* or *Polysyncraton lithostrotum*	191681-63-7	cancer/ not reported	tubulin binding agent	cell culture; IC50's of 6-311 nM (panel of tumor cell lines HCT116 cells, A549 cells, SK-MEL-5 cells A498 cells). The increase in lifespan (ILS) for CDF1 mice after ip injection of P388 tumor cells was in the range of -45 to +70% over the dose range of 0.13 to 0.006 mg/kg.

FIG. 11W

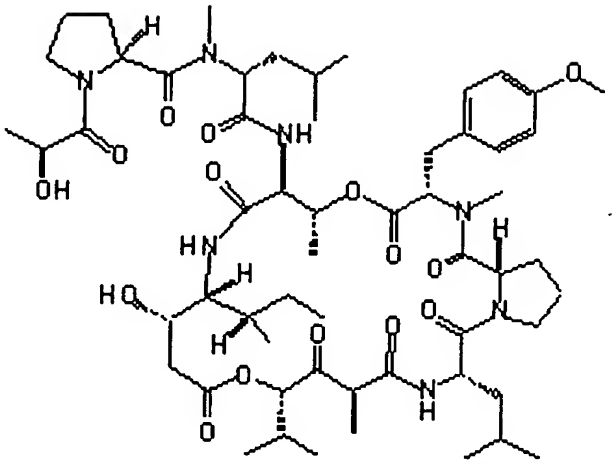
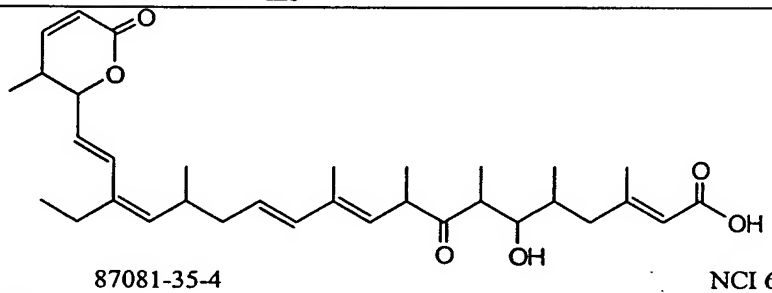
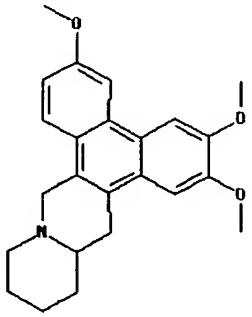
				
Didemnin B/ *Tridemnum solidum*/ NSC-2325319; IND 24505	77327-05-0; 77327-04-9; 77327-06-1/ other related natural products	non-Hodgkin's lymphoma, breast, carcinoma, CNS, colon/ Discontinued due to cardiotoxicity; nausea, neuro-muscular toxicity and vomiting MTD 6.3 mg/Kg; toxicity prevented achieving a clinically signif. effect; rapidly cleared (t1/2 4.8 hrs	inhibits protein synthesis via EF-1	NCI 60-tumor panel (GI50's): 100 nM to 50 fM. Not potent against MDR cell lines.
				
Leptomycin B/ *Streptomyces* sp. strain ATS 1287/ NSC-364372; elactocin	87081-35-4			NCI 60-tumor panel (GI50's): 8 μM to 1 pM; (LC50): 250 μM to 10 nM (several cell lines at 0.1 nM). Two testing results with very different potencies.
				
Cryptopleurin/				NCI 60-tumor panel

FIG. 11X

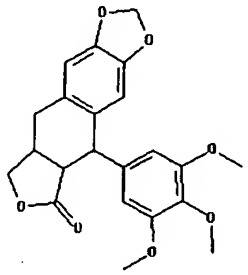
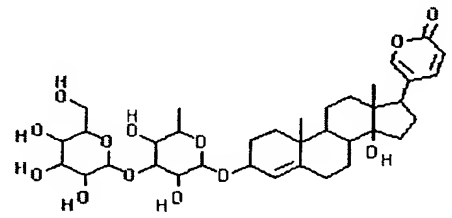
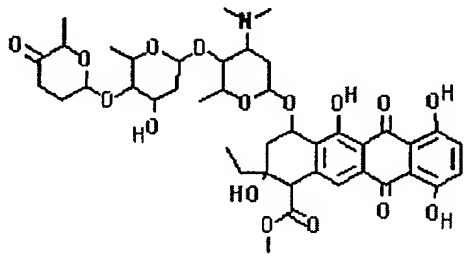
not known/ NSC-19912		(GI50's): 19 nM to 1 pM; (LC50): 40 μM to 10 nM (several cell lines at 1 pM).
		
Silicicolin/ not known/ NSC-403148, deoxypodophyllotoxin, desoxypodophyllotoxin podophyllotoxin, deoxysilicicolin	19186-35-7	NCI 60-tumor panel (GI50's): ~100 nM to 3 nM; (LC50): 50 μM to 10 nM
		
Scillaren A/ not known/ NSC-7525; Glucoproscillaridin A; Scillaren A	124-99-2	NCI 60-tumor panel (GI50's): 50 nM to 0.1 nM; (LC50): 250 μM to 0.1 nM
		
Cinerubin A-HCl/ not known/ NSC-243022; Cinerubin A hydrochloride; CL 86-F2 HCl; CL-86-F2-hydrochloride	not reported	NCI 60-tumor panel (GI50's): 15 nM to 10 pM; (LC50): 100 μM to 6 nM

FIG. 11Y